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# Magnetic Resonance Imaging of the Brain: Relationship Between Structure and Function

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## INTRODUCTION

Computerized tomography (CT) of the brain, which was introduced in the 1970s, revolutionized neurologic assessment [1]. This revolution continued with the introduction of magnetic resonance (MR) imaging (MRI) in the 1980s and further expanded with improvements in such other imaging methods as functional MR imaging (fMRI), single photon emission tomography (SPECT), and positron emission tomography [2]. In the early development of both CT and MR technology, image-acquisition and technical limitations meant that image display was always two-dimensional. Limitations in quantitative methods relegated most studies to simple linear measurements of a brain region or structure on a given slice [3]. In addition, because of constraints in obtaining sufficient numbers of scan slices for clinical interpretation but limiting the amount of patient time in the scanner to tolerable limits, slice thickness and distance between the next slice were often less than optimal for research purposes. Thus, in the early stage of clinical neuroimaging, interpolation of what may be at a given level was ever present, and three-dimensional (3-D) image analysis had to be performed in the ''mind's eye'' rather than through some technologic approach [4]. Fortunately, all of that has changed in dramatic fashion, with current capabilities of exquisite 3-D displays of brain and pathology. This type of image analysis also has yielded a means by which function can be related to structure. This article provides a description of such methods along with depictions of 3-D brain imaging and the use of such volumetric techniques in studying neuropsychological outcome following brain damage.

## TRACING, THRESHOLDING, AND SEGMENTATION

The first step in 3-D image display is to isolate the structure(s) of choice. Typically, this is performed by one technique or by a combination of techniques: tracing, thresholding, and/or segmentation. With the simple threshold technique, because the MR image is already displayed on a gray scale, each pixel is represented by a value on the 256 different levels of gray. The threshold technique groups pixels together within a certain range, which then permits their isolation from other pixels of differing gray-scale value. This is demonstrated in Figure 1. For example, to isolate the ventricle, the range of pixel values found within the ventricular space is identified. Thresholding programs are based on an algorithm that expands the boundary of similar pixel values (within a defined range) to an edge where clearly different pixel values exist. Thus, as depicted in Figure 1, the range of pixel values is established within the ventricle based on the pixel values within the cerebrospinal fluid (CSF) space of the ventricle. By using that range, thresholding permits the determination at that slice level of the surface area within the range of pixel values identified as CSF. The thresholding method used in our work and depicted in Figure 1 is based on the thresholding software NIH Image (Bethesda, MD) [5]. This program is in the public domain and can be downloaded at the following ftp address: zippy.nimh.nih.gov. Additional information about this image-analysis program can be obtained from the following http address: htpp://rsb.info.nih.gov/nih-image/. Some structures, such as the corpus callosum, as depicted in Figure 2, have such distinct boundaries that simple tracing techniques can be applied. In such cases, a computerized tracing routine is used in which the trace is under operator control or in which a combination of simple thresholding followed by tracing is employed.

The problem with thresholding and tracing techniques is that, typically, they have to be carried out separately at each individual slice level. Segmentation methods, however, may be applied to multiple slices; therefore, they are often preferred for performing many image-analysis tasks. Also, the segmentation process may utilize less operator input, which tends to make it a more reliable method with reduced likelihood for operator error. In the segmentation process, two coregistered MR images of different weights are used–typically, mixed-weighted or proton-density and T2-weighted images (see Fig. 3). By having the images coregistered and of different sensitivities, delineation of tissues that differ in their signal intensity can be achieved readily (see Fig. 3). Typically, for imaging brain tissue, the segmentation method can be

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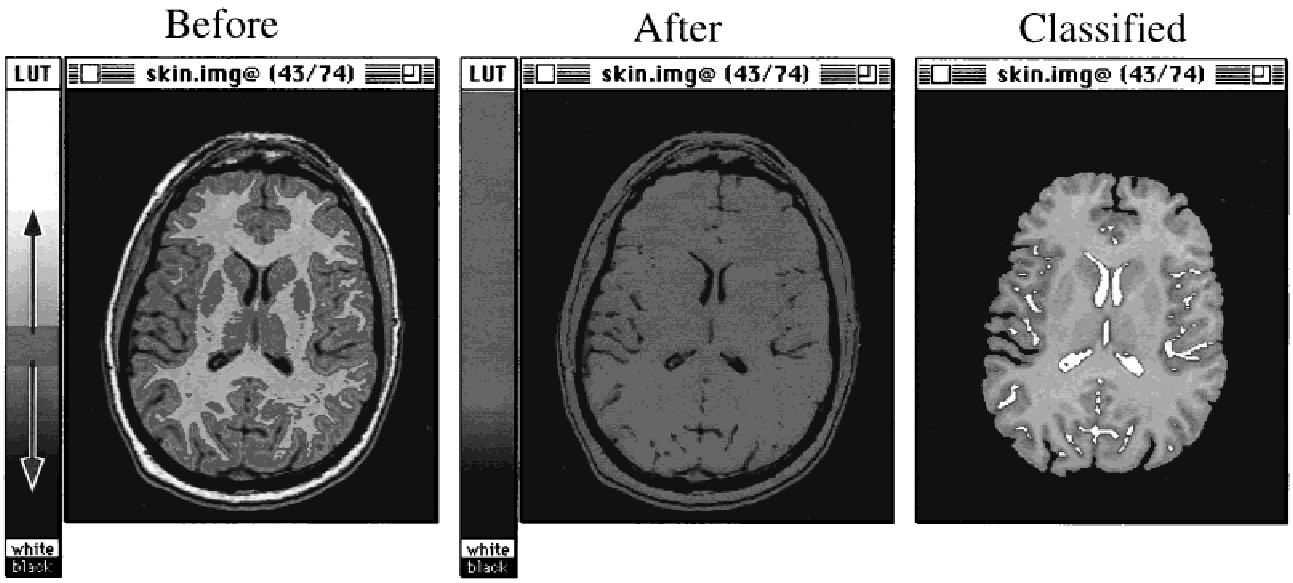


**Fig. 1.** Typical ''thresholding'' sequence using Image software. **Before:** Axial image at level of the anterior horn of the lateral ventricle. **After:** The same axial image from the before image, but the ventricle has been isolated, and all other brain parenchymal tissue has been given a similar value on the gray scale. Note that this thresholding technique essentially isolates cerebrospinal fluid (CSF) from brain, and each of those compartments results in a uniform pixel classification. **Classified:** The classified image takes the uniform pixel classification of the ventricular system and is now superimposed on the original axial image, so that the ventricle can be isolated from other brain structures. By performing this type of analysis at all levels of the ventricular system, not only can the surface area of the ventricle be calculated at each level, but the volume of the ventricle can be calculated.

used to separate whole brain from bone/meninges and, within brain parenchyma, to separate white matter from gray matter and to separate both from CSF-filled spaces. The segmentation program used in our work and depicted in Figure 3 is based on the Mayo Clinic program Analyze [6].

## 3-D DISPLAY OF BRAIN STRUCTURE

By using the above-mentioned techniques, an almost limitless number of displays can be generated. For example, Figure 4 depicts 3-D reconstructions of the head of a child who sustained a serious, traumatic brain injury with frontal fracture and anterior-inferior frontal lobe contusion, resulting in permanent encephalomalacic change. First, the 3-D reconstruction of the head is depicted, followed by a stripping away of the skin, muscle, fascia, bone, and meninges to uncover the surface of the brain. Next, the lesion is isolated and presented in multiple perspectives.

Figure 4 depicts how a particular lesion can be viewed in 3-D. The same techniques can be applied to a structure as well. For example, the hippocampus is a structure that is often injured in cerebral trauma and can be isolated with segmentation and tracing techniques, as depicted in Figure 5. Because the hippocampus is such an irregular structure, it is sometimes difficult to visualize in a singular plane. Figure 5 shows clearly that, by examining the 3-D view of the hippocampus in this patient with traumatic brain injury, significant size reduction in the hippocampus has occurred.

Like the depiction of the hippocampus (Fig. 5), exquisite, 3-D views of any intricate and complex structure can be presented, such as the ventricular system presented in Figure 6. In this illustration, the ventricle is presented in any plane desired and can be presented in isolation or within its position in the skull or brain. The importance of 3-D imaging of the ventricular system is that ventricular changes are commonplace in a variety of pathologic conditions, and they provide a good index of brain pathology [3]. Numerous studies have demonstrated the utility in using ventricular measures as indices of brain pathology in examining neuropsychological outcome [7–10].

## QUANTITATIVE NEUROIMAGING AND CLINICAL APPLICATION

By using the techniques described above–tracing, thresholding, and segmentation–a variety of quantitative measures can be obtained of specific or whole brain structures. For example, Blatter et al. [11] have provided normative data for individuals 16–65 years of age on a

**Fig. 2.** Magnetic resonance (MR) midsagittal view of the brain depicting tracing of the corpus callosum following a thresholding procedure to isolate the corpus callosum from the rest of the brain. This illustration also demonstrates a simple, anterior-to-posterior, linear measurement of intracranial distance that can be used as a correction factor to correct for head size differences [15].

variety of brain parameters. By providing such normative standards, deviations related to some pathologic change can be documented readily. For example, in the patient presented in Figures 5 and 6, it is apparent that there has been significant brain wasting and ventricular enlargement (hydrocephalus ex vacuo) as a consequence of severe, traumatic brain injury. However, what is the magnitude of this change? Such an estimate is difficult to gauge with only simple visualization of the scan, although it is evident that substantial differences are present. In contrast, by performing a quantitative analysis, as illustrated in Figure 7, it is apparent that the changes that occur exceeded several standard deviations (see ventricle-to-brain ratio comparisons; Fig. 8) from the normal base line as well as from the patient's base line.

This quantitative analysis also provides an opportunity to examine structure-function relationships. For example, the ventricular changes demonstrated in Figure 7 following traumatic brain injury have been well documented since the first systematic study of trauma after the advent of CT imaging in the 1970s [12]. Parenchymal damage often results in ventricular expansion, because, as brain tissue degenerates, the brain looses volume. Because CSF within the walls of the ventricle is under pressure,

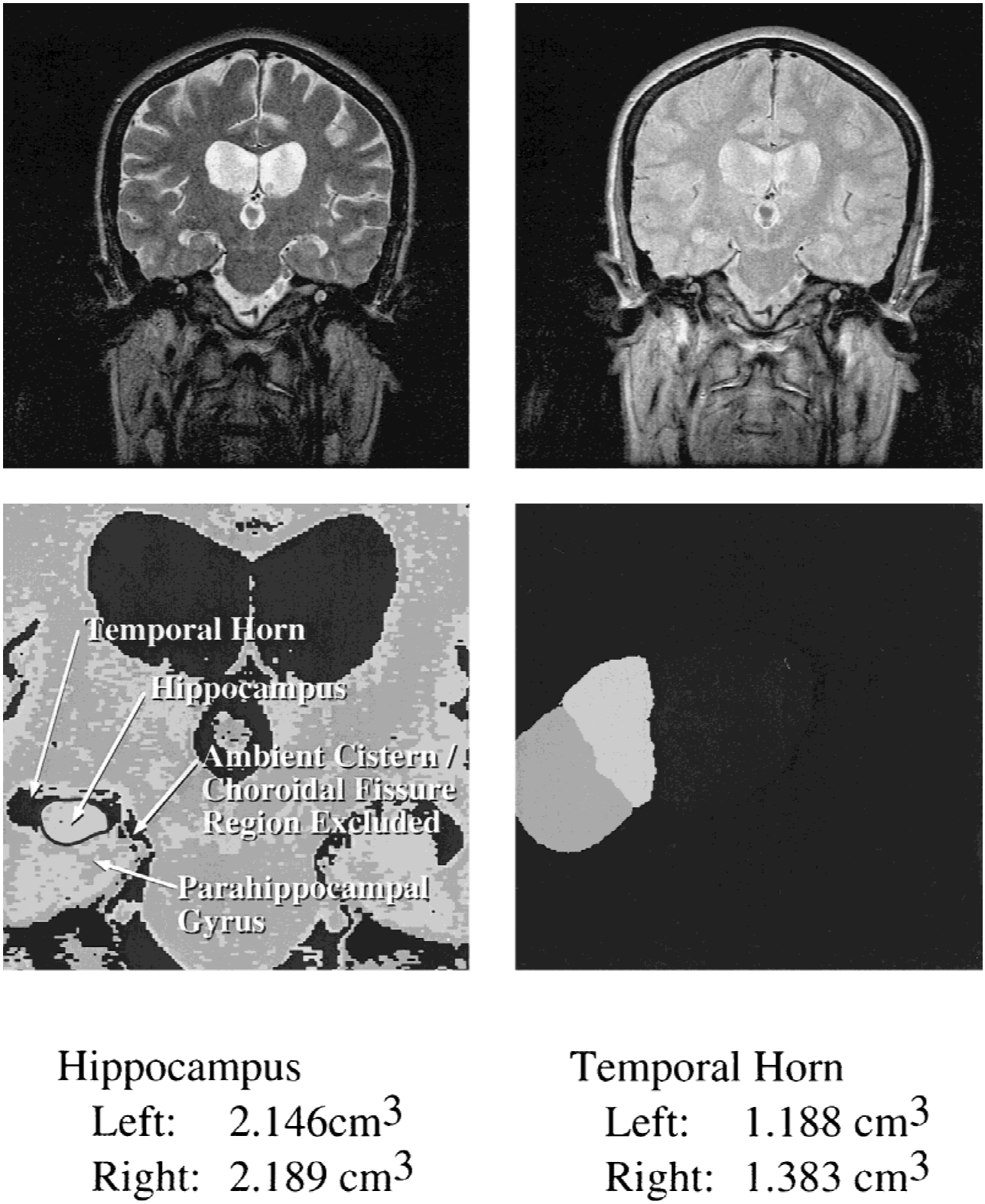


**Fig. 3.** Typical segmentation routine utilized for quantitative image analysis of the brain. **Top:** T2-weighted MR scan in the coronal plan at the level of the hippocampus (left). Coregistered proton-density scan at the identical level (right). **Bottom:** Feature space map that plots the T2-weighted image against the proton-density image, which yields the ''space'' of common pixel values for a particular tissue (right). Segmented image depicting the isolation of the hippocampus and temporal horn of the lateral ventricle from the rest of the brain for the purposes of volumetric quantification (left). By using this technique, the calculated hippocampal and temporal horn volumes for this patient are shown at the bottom.

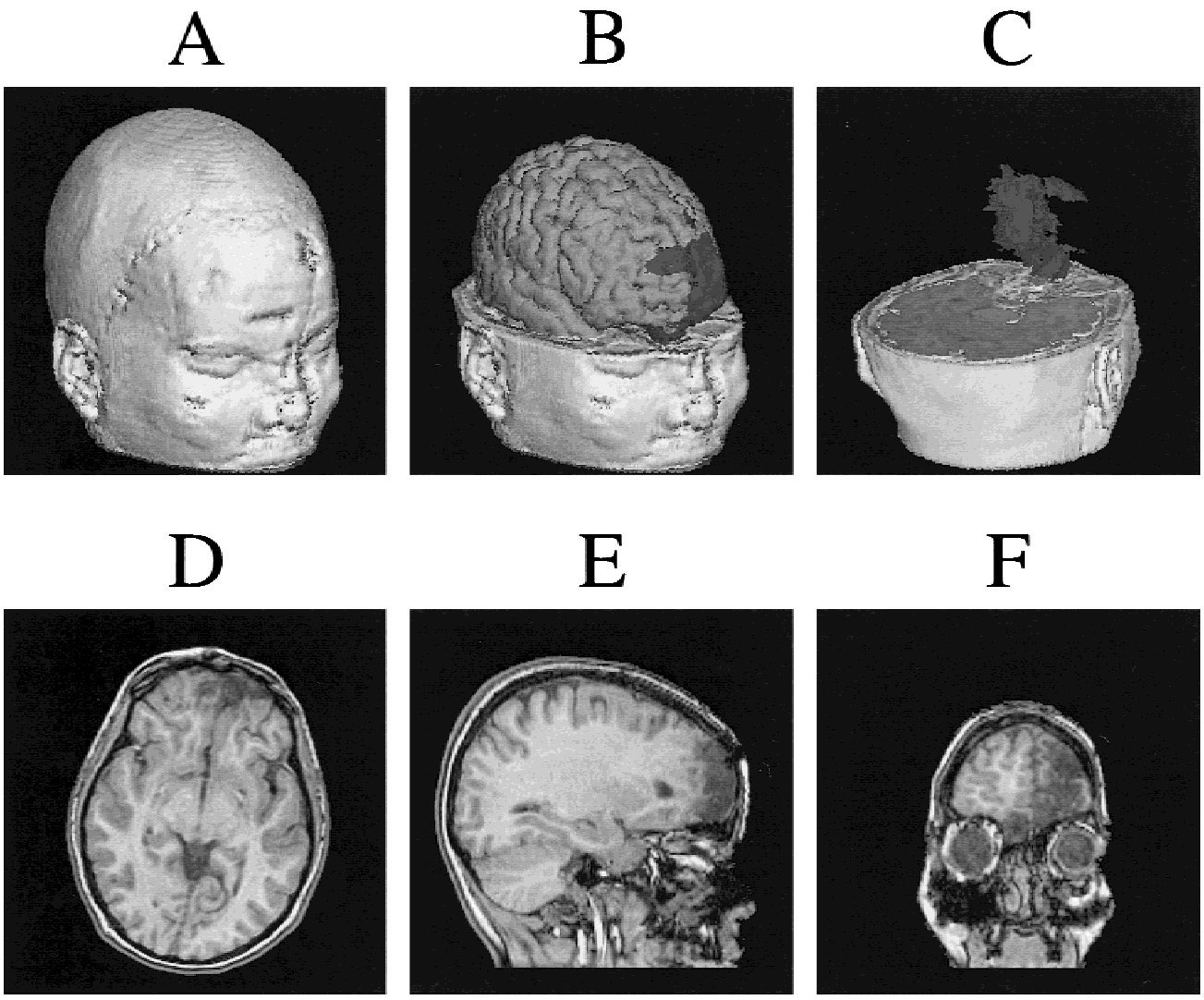


**Fig. 4.** Three-dimensional (3-D) image analysis. **A:** 3-D depiction of the head based on MR in a child who sustained a serious traumatic brain injury. Note the residual craniotomy scar as well as the soft-tissue and bony defect in the left frontal region. **B:** By using a combination of thresholding and segmentation techniques, the cortical surface of the brain is isolated from the meninges and cortical bone, and the lesion in the frontal region, particularly in the left frontal area, is isolated. **C:** The frontal lesion is further isolated from the rest of the brain and can be presented in any 3-D position. **D–F:** Original axial, sagittal, and coronal MR images depicting the position of the lesion.

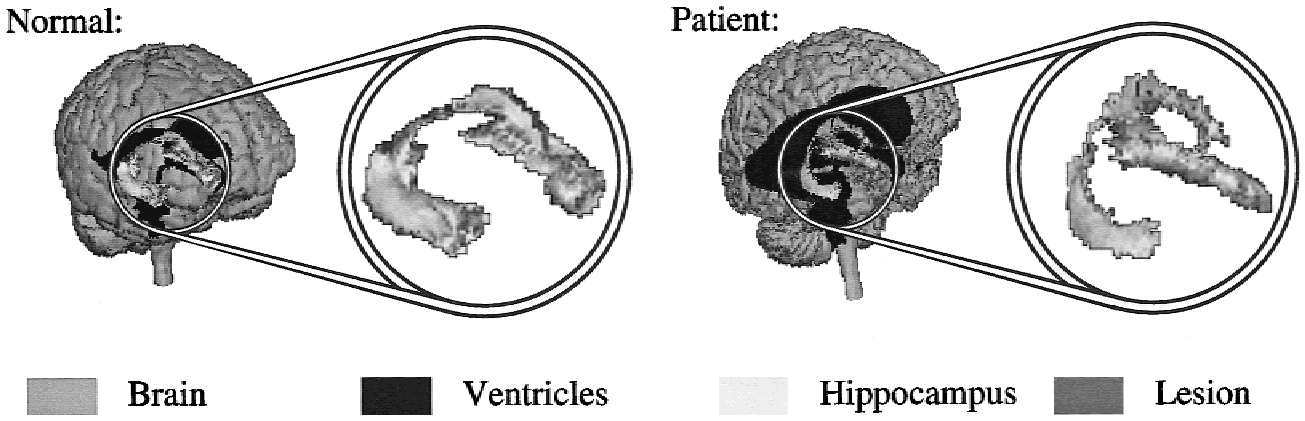


**Fig. 5.** By using the techniques discussed in Figure 4, this patient's MR scan is segmented in a manner that highlights and extracts the hippocampus and fornix, and these structures are compared in 3-D to a normal, nonbrain injured subject. Note the size reduction in both the hippocampus and the fornix in this subject. This illustration demonstrates that even odd-shaped structures, like the hippocampus, can be isolated and studied by using these 3-D techniques. Another irregular-shaped structure—the ventricular system—is depicted in Figure 6.

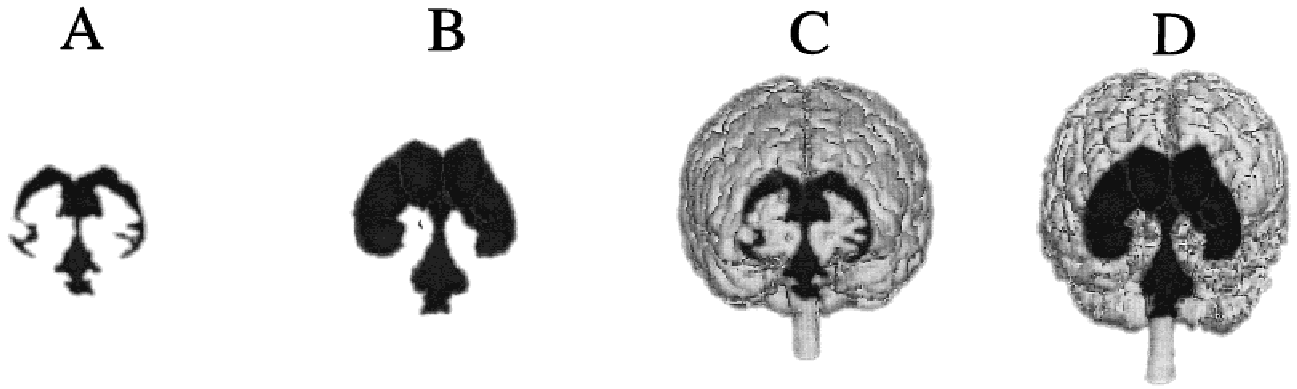


**Fig. 6. A–D:** 3-D imaging of the ventricular system in a normal individual (A,C) compared with an individual with traumatic brain damage (B,D). The size of the ventricle relates to the degree of pathologic change and neuropsychological outcome. Typically, the larger the ventricular expansion in response to tissue loss, the greater the neuropsychological deficit.

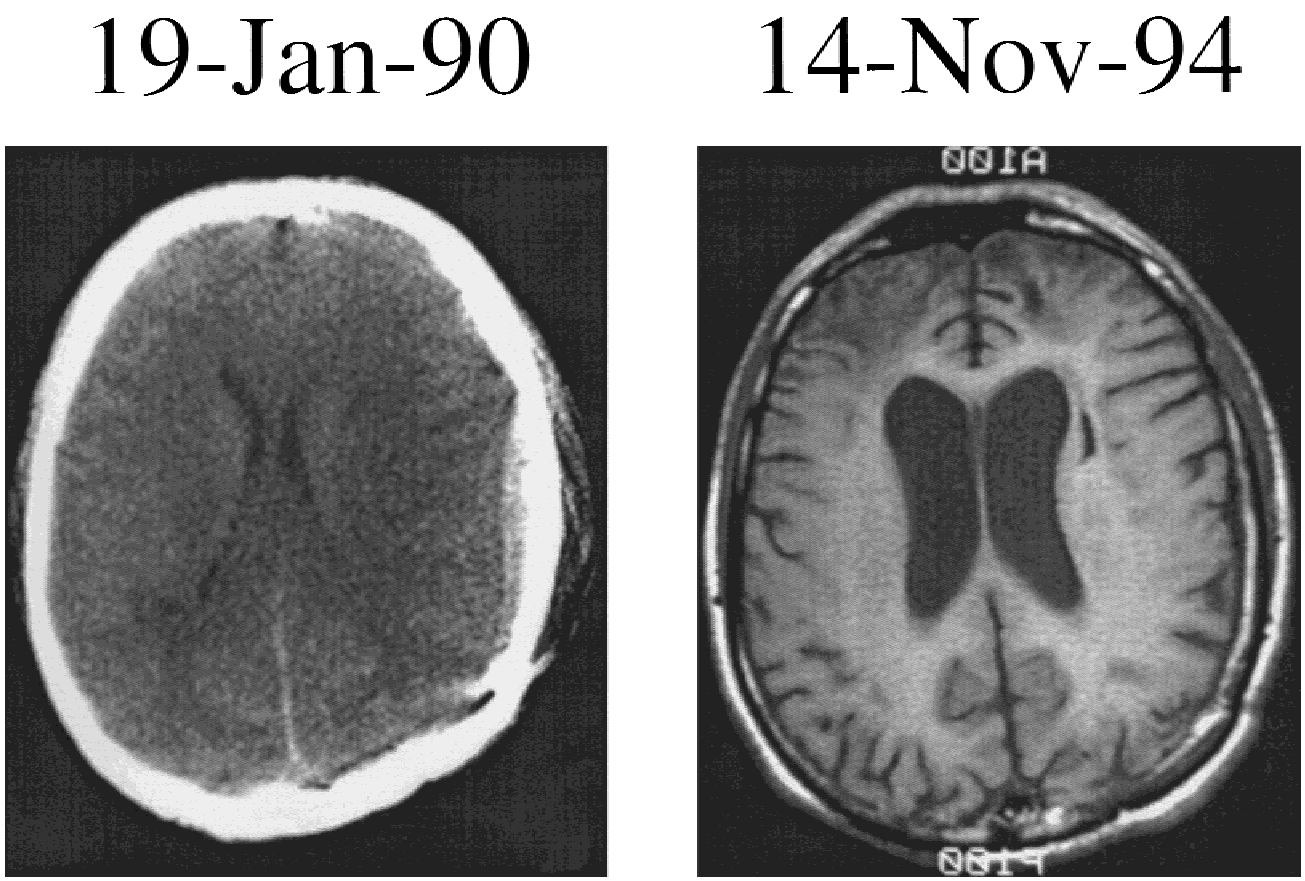


**Fig. 7.** Day-of-injury (DOI) computed tomography (CT) scan (19-Jan-90) in a trauma victim (fall of some 30 feet). Note the presence of skull fracture in the posterior right quadrant (scans are presented with the patient's left on the viewer's left). Adjacent to the DOI scan is a follow-up MR scan (14-Nov-94) several years postinjury that demonstrates ventricular dilation, cortical atrophy, and a lesion adjacent to the right body of the lateral ventricle. These pathological changes are typical of severe trauma to the brain and can be quantified, as depicted in the histogram presented in Figure 8.

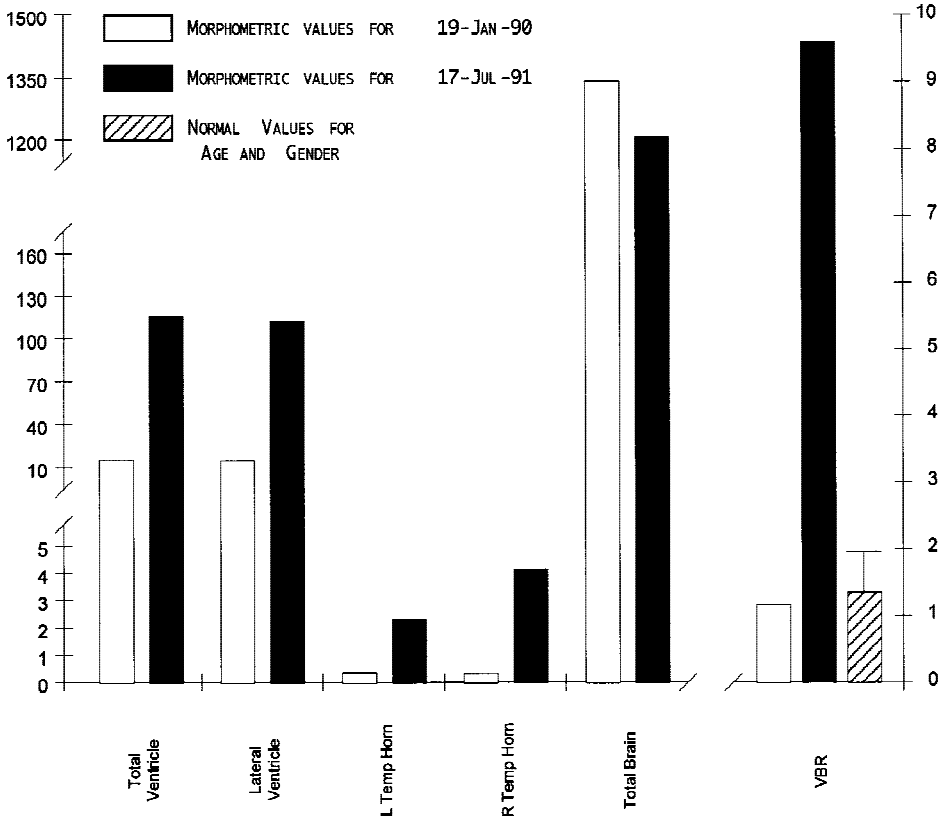


**Fig. 8.** Histogram of brain morphometrics following brain injury. The open histogram represents DOI values, and, in comparison, the follow-up scan demonstrates marked atrophic reaction to the injury (dark histogram), as manifested by increased ventricular size and elevated ventricle-to-brain ratio (VBR). An additional comparison is made with the VBR to a normative data base [16]. It can be seen from the DOI scan that VBR is within normal limits compared with the normative sample. Thus, the DOI comparison is a good representation of the brain before the ensuing pathological responses to trauma. The change in the brain from DOI to follow-up may be the most significant indicator of pathologic change [7].

any loss of brain substance results in passive ventricular expansion, because brain parenchymal volume is the factor that maintains ventricular size, provided that there is normal intraventricular pressure. Because ventricular changes are observed so reliably as long-term consequences in cerebral trauma, a number of structure-function studies have been published [7]. The general finding of these studies is that ventricular expansion, as an index of severity of brain damage following trauma, is related to worse outcome. Thus, in a general sense, the greater dilatation of the ventricular system, as an indicator of parenchymal wasting, is associated with worse neuropsychological outcome, particularly dilation of the temporal horn [13]. This research also has examined specific structures, such as the hippocampus, which has a known role in memory function [14]. Traumatic brain injury results in nonspecific changes in hippocampal volume, which, in turn, relate in a very modest fashion to memory performance on neuropsychological tests [13].

## SUMMARY

Contemporary brain-imaging methods permit exquisite 2-D and 3-D image analyses that can result in quantification of any given structure, lesion, or pathological state provided certain pixel boundaries can be identified on the computerized image. Several examples of the methods for image analysis and their display are provided here along with a review of the literature on their clinical and empirical use.

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